ANNALS OF SURGERY
Vol. 217, No. 5, 447–457

Chemical Splanchnicectomy in Patients with Unresectable Pancreatic Cancer

A Prospective Randomized Trial

Keith D. Lillemoe, M.D., John L. Cameron, M.D., Howard S. Kaufman, M.D., Charles J. Yeo, M.D., Henry A. Pitt, M.D., and Patricia K. Sauter, R.N.

From the Department of Surgery, The Johns Hopkins Medical Institutions, Baltimore, Maryland

Objective

A prospective, randomized, double-blind study was completed comparing intraoperative chemical splanchnicectomy with 50% alcohol versus a placebo injection of saline in patients with histologically proven unresectable pancreatic cancer.

Methods

Standardized assessment of pain, mood, and disability due to pain was completed preoperatively and at 2-month intervals until death. Chemical splanchnicectomy with alcohol was performed in 65 patients, whereas 72 patients received the placebo. The two groups were similar with respect to age, sex, location, and stage of tumor, operation performed, the use of postoperative chemo- and radiation therapy, and initial assessment scores for pain, mood, and disability.

Results

No differences in hospital mortality or complications, return to oral intake, or length of hospital stay were observed. Mean pain scores were significantly lower in the alcohol group at 2-, 4-, and 6-month follow-up and at the final assessment ($p<0.05$). To further determine the effect of chemical splanchnicectomy, patients were stratified into those with and without preoperative pain. In patients without preoperative pain, alcohol significantly reduced pain scores and delayed or prevented the subsequent onset of pain ($p<0.05$). In patients with significant preoperative pain, alcohol significantly reduced existing pain ($p<0.05$). Furthermore, patients with preexisting pain who received alcohol showed a significant improvement in survival when compared with controls ($p<0.0001$).

Conclusion

The results suggest that intraoperative chemical splanchnicectomy with alcohol significantly reduces or prevents pain in patients with unresectable pancreatic cancer.

Carcinoma of the pancreas has increased steadily in incidence over the last 50 years. In the United States, it was estimated that over 28,000 new cases were diagnosed in 1991.[1] Unfortunately, at the time of diagnosis most patients with pancreatic cancer are unresectable for cure. Thus, optimal palliation of symptoms, to maximize the quality of life is of primary importance in the majority of patients. Significant improvement in the sur-

gical palliation of pancreatic carcinoma has been achieved in recent years.[2-5] Furthermore, nonoperative palliation of obstructive jaundice has been demonstrated to effectively relieve this symptom in patients deemed to be inoperable based either on extent of disease or general medical condition.[6-9] Yet, perhaps the most disturbing and incapacitating symptom of pancreatic cancer, pain, is poorly managed, and can remain a significant problem for many patients until death.

The use of chemical splanchnicectomy in patients with unresectable pancreatic cancer was first described by Copping and colleagues in 1969.[10] This group expanded their experience to 41 patients in a report in 1978.[11] Since that report, other authors have advocated chemical splanchnicectomy for palliation of pain due to unresectable pancreatic cancer.[12,13] Yet, despite these reports, a prospective, randomized, placebo-controlled study of this treatment has never been performed. Moreover, a standardized, quantitative assessment of pain has never been used to measure pain control after chemical splanchnicectomy. Finally, the question of prophylactic use of chemical splanchnicectomy in patients with unresectable pancreatic cancer without pain at the time of laparotomy has never been addressed.

This double-blind study was designed to prospectively compare chemical splanchnicectomy with alcohol versus saline placebo using random assignment in patients found to have unresectable pancreatic carcinoma at laparotomy. We believe that this study represents the first ever reported prospective, randomized, placebo-controlled trial for the management of pain resulting from pancreatic cancer.

METHODS

Between February 1987 and December 1991 all patients with suspected pancreatic carcinoma who were to undergo surgical exploration for either resection or palliation were interviewed preoperatively. After obtaining informed consent, as approved by the Joint Committee of Clinical Investigations at the Johns Hopkins Hospital, patients underwent preoperative assessment using a standardized questionnaire. The presence or absence of pain and its location were determined. A quantitative assessment of the use of pain medications (both narcotic and non-narcotic), and other medications such as tranquilizers, muscle-relaxants, antidepressants, and hypnotics was obtained. Patients were then instructed to rate the extent of their pain, overall disability due to pain, and mood by a visual analogue scale (Fig. 1).

VISUAL ANALOGUE SCALE

1. How severe is your pain now?

No Pain _____ Unbearable Pain

2. How much is pain now interfering with your activities?

Not at all _____ Completely Disabled

3. What is your mood like now?

Best ever felt _____ Worst ever felt

Figure 1. Visual analogue scales used for measurement of pain, mood, and disability due to pain. The patient was instructed to mark across each scale with a single line at the point representing their response to the question. Each line is 10 cm long. The distance of marked point was measured from left and the distance represented the visual analogue score on a scale of 0–10.

All patients underwent surgical exploration with operative management including biopsy of the tumor, determination of resectability, and the performance of palliative biliary and gastrointestinal bypass as determined by the attending surgeon. Patients with histologically proven unresectable pancreatic adenocarcinoma were then randomized to receive chemical splanchnicectomy with either 50% alcohol in saline or normal saline (0.9%) placebo. Those patients in whom the pancreatic tumor was resectable or in whom the diagnosis of pancreatic adenocarcinoma could not be confirmed histologically were excluded from the study. Chemical splanchnicectomy was performed by the operating surgeon by the injection of 20 cc of either the 50% alcohol or saline solution on each side of the aorta at the level of the celiac axis using a 20- or 22-gauge spinal needle (Fig. 2). The attending surgeon, assistants, and the patient were unaware of the content of the solution, which had been prepared by an operating room nurse.

Postoperative management was directed entirely by the surgical staff. Routine postoperative pain control including parenteral or oral narcotics administered as needed and patient-controlled analgesia via intravenous administration of morphine was used in all patients. Hospital course was monitored for postoperative complications, return of bowel function, and length of hospital stay. Before hospital discharge, all surviving patients underwent repeat pain assessment using the same questionnaire that was used in the preoperative assessment.

Supported by NIH grant RO1-CA-49776.
Presented at the 104th Annual Meeting of the Southern Surgical Association, Aventura, Florida, December 7, 1992.
Address reprint requests to Keith D. Lillemoe, M.D., Department of Surgery, The Johns Hopkins Hospital, 600 N. Wolfe Street, Blalock 603, Baltimore, MD 21287-4606.
Accepted for publication January 11, 1993.

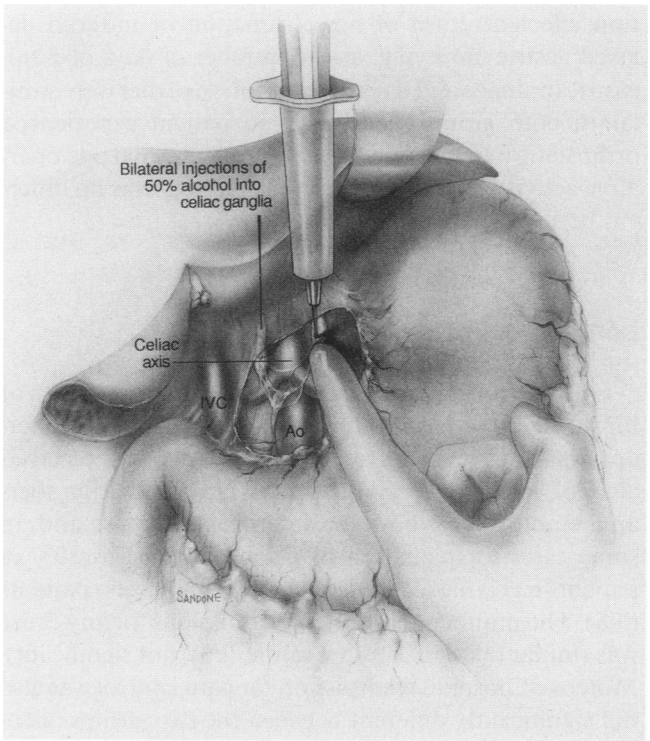

Figure 2. Chemical splanchnicectomy was performed using a syringe and a 20- or 22-gauge spinal needle. Solution (20 cc) was injected on each side of the aorta (AO) at the level of the celiac axis (IVC = inferior vena cava).

After hospital discharge, the management of the patient was directed entirely by his or her treating physicians. The use of pain medications, referral for chemo- and or radiation therapy, and performance of percutaneous celiac axis block for pain control were made independently of the study. All patients and treating physicians remained blinded as to the randomization status. Follow-up questionnaires were completed either by direct interview or by mail for all patients at 2-month intervals until the death of the patient. In many cases, personal contact was made with the patient by telephone to ensure accuracy of the questionnaire and to determine the overall status of disease and treatment. If a percutaneous celiac axis block was performed, the patients continued to complete the questionnaires; however, the results after this procedure were not included in data analysis. In all other cases, including patients receiving chemo- or radiation therapy, data were collected and analyzed until death.

Patients were stratified for analysis based on the presence or absence of pain before laparotomy for pancreatic cancer. Patients were classified as having significant preoperative pain if their initial pain assessment score was greater than or equal to 3 on the visual analogue scale of 0–10. This score was chosen because, in general, patients with pain scores at this level required narcotic pain medications, whereas patients with lower scores rarely required narcotics. This arbitrary point was also used to assess the extent of pain during follow-up. All narcotic use was standardized to the morphine equivalents by the method described by Grossman and Scheidler.[14] Significant narcotic use was considered to be present for any patient taking greater than or equal to 10 mg IM of morphine sulphate equivalent per day.

Pain, mood, and disability scores were compared over time and between alcohol and saline groups for all patients and the subgroups of patients with and without preoperative pain. Paired data for individual patient pain, mood, and disability scores were compared between preoperative and 2-, 4-, and 6-month intervals using Wilcoxon signed-rank tests. Scores were then compared between alcohol and saline treatment groups at each interval by the Mann-Whitney rank test. Standard demographic and treatment data were compared between treatment groups by independent Student's *t*-tests. The incidence of specific pre- and postoperative variables were compared by Chi-square analysis. Estimates for survival were compared using the method of Kaplan and Meier.[15]

RESULTS

A total of 371 patients with suspected pancreatic carcinoma underwent preoperative assessment. Two hundred and thirty-two patients were excluded from this study because of either a resectable periampullary neoplasm (N = 202) or a benign inflammatory condition (N = 30). Thus, 139 patients underwent randomization after intraoperative findings of unresectable pancreatic adenocarcinoma were confirmed histologically. Two patients were excluded from chemical splanchnicectomy by the attending surgeon because extensive tumor in the area of the celiac axis precluded safe injection. In all, 137 patients underwent celiac axis injection, with 65 patients receiving 50% alcohol and 72 patients receiving the saline placebo.

Patient Characteristics

No significant differences in patient age, sex, symptoms at the initial examination, tumor location, or operation performed were observed between the alcohol and placebo groups (Table 1). The findings of liver metastases or peritoneal metastatic implants (Stage IV) precluded resection in 40% and 35% of the patients receiving alcohol and saline, respectively (not significant). Extensive local disease (Stage III), primarily with involvement of the superior mesenteric vein, portal vein, or the superior mesenteric artery precluded resection in

Table 1. PATIENT CHARACTERISTICS

	Alcohol (N = 65)	Placebo (N = 72)
Age (mean)	64.0 years	63.9 years
% Male	60%	57%
Symptoms		
Weight loss	62%	67%
Jaundice	55%	51%
Anorexia	37%	36%
Vomiting	22%	24%
Tumor location		
Pancreatic head	74%	75%
Pancreatic body or tail	26%	25%
Reason not resected		
Local involvement (Stage III)	60%	64%
Metastatic disease (Stage IV)	40%	35%
High risk	0%	1%
Operative management		
Biliary bypass & gastrojejunostomy	63%	64%
Gastrojejunostomy (alone)	14%	22%
Exploration & biopsy	17%	13%
Operative time (mean)	4.3 hrs.	4.1 hrs.
Estimated blood loss (mean)	1.5 units	1.8 units
Intraoperative blood transfusions (mean)	308cc.	321cc.

There were no significant differences for any of these parameters between the alcohol and the placebo groups.

all but one of the remaining patients. Advanced medical illness and high operative risk precluded tumor resection in one patient receiving placebo injection.

The length of the operation, estimated intraoperative blood loss, and units of blood transfused intraoperatively were not significantly different between the two groups. The length of time required to perform chemical splanchnicectomy was not specifically measured, but is estimated to be about 5 minutes per patient. Two transient hypertensive events without sequelae occurred during alcohol celiac axis injection, both were presumed to be associated with adrenal injection. No hypotensive episodes were observed following any celiac axis injection, nor was bleeding observed at the site of injection in any patient.

Postoperative Course

The postoperative course of patients receiving alcohol and saline is shown in Table 2. There were a total of six hospital deaths (4.4%), including two patients who received alcohol (3.1%) and four patients who received saline (5.6%) (not significant). There were no differences in the overall incidence of complications or for any specific complication. There was no evidence that alcohol injection affected return of bowel function or induced delayed gastric emptying, as the number of days of nasogastric drainage and days to resumption of diet were similar in both groups. Similarly, no patient experienced orthostatic hypotension upon return to normal postoperative activity. Finally, overall hospital stay was no different between the two groups.

Long-term Follow-up

Follow-up was completed on all patients until death or for surviving patients until October 1, 1992. Chemotherapy was administered to 16% of patients who received alcohol, and 12% receiving saline (NS). Radiation therapy, employed for both local control of disease and, in some cases for palliation of pain, was used in 19% of patients receiving alcohol and in 29% of placebo patients (NS). The number of hospital readmissions for any cause was similar (alcohol 11% vs. saline 18%, not significant). Moreover, hospital readmission for pain control was also not significantly different between the two groups (alcohol 3% vs. saline 9%). Finally, 10% of patients who received an intraoperative chemical splanchnicectomy with alcohol required percutaneous celiac axis block for significant pain compared with 12% of patients in the control group. Although this difference was not significant, the average number of months in the alcohol group between operative chemical splanchnicectomy and percutaneous celiac block was 11.8 ± 3.2 versus 4.0 ± 1.1 months for the control patients ($p < 0.05$). All patients receiving postoperative percutaneous celiac axis block with alcohol reported a significant improvement in pain scores.

Table 2. POSTOPERATIVE COURSE

	Alcohol (N = 65)	Saline (N = 72)
Hospital mortality	3.1%	5.6%
Any complication	35%	34%
Wound infection	12%	8%
Cholangitis	9%	11%
Biliary anastomotic leak	3%	3%
Pneumonia	3%	3%
Cardiac event	5%	4%
Length of nasogastric drainage	5.0 days	6.0 days
Days until oral intake	6.8 days	6.9 days
Days until regular diet	9.2 days	9.3 days
Postoperative length of stay	13.8 days	13.9 days

There were no significant differences for any of these parameters between the alcohol and the placebo groups.

Table 3. INITIAL PATIENT ASSESSMENT FOR ALL RANDOMIZED PATIENTS

N	Alcohol (N = 65)	Placebo (N = 72)
Current pain	2.1 ± .3	2.0 ± .3
Mood	4.8 ± .3	4.3 ± .2
Disability	2.9 ± .4	2.4 ± .3

Range: 0–10, see Figure 1.

Initial Patient Assessment—All Randomized Patients

The results for initial assessment of current pain, mood, and disability due to pain for all randomized patients is shown in Table 3. There were no significant differences in the mean scores for pain, mood, or disability between the two groups. The location of pain was described as being abdominal and/or back pain in all patients. At the time of the initial assessment, 37 patients (27%) were considered to have significant pain based on a score of 3 or greater on the visual analogue scale. Twenty of these patients were randomized to receive alcohol and 17 to receive saline placebo. The proportion of patients receiving alcohol with significant pain was 31% vs. 24% for saline (not significant). No difference in the preoperative use of narcotic pain medications was observed between the two groups (alcohol 20% vs. saline 18%).

Follow-up Pain Assessment—All Randomized Patients

Mean visual analogue pain scores are shown for all randomized patients at the preoperative, 2, 4, and 6 month and final assessments (Fig. 3). Compared to saline placebo, alcohol significantly reduced the mean pain score for surviving patients at the 2, 4, and 6 months. The final pain assessment score, performed within two months of death, was also significantly lower in the alcohol group.

Paired analysis was performed comparing preoperative pain assessment with the 2, 4, and 6 month assessment scores for all patients alive at each assessment point (Table 4). This analysis demonstrated that patients receiving placebo injection had a significant increase in pain scores compared to the preoperative level beginning at the 2 month assessment. In contrast, patients receiving alcohol had no significant change from their initial pain assessment score at either 2 or 4 months. Only at the 6 month assessment did patients receiving alcohol have a significant increase in pain score compared to their initial assessment.

Pain Assessment in Patients with No Preexisting Pain

Mean pain assessment scores at the preoperative, 2-, 4-, and 6-month and final assessment points for those patients without preexisting pain are shown in Figure 4. The mean pain scores in the alcohol group at 2 and 6 months and at the final assessment were significantly lower and also approached statistical significance at 4 months when compared with saline placebo. Paired analysis for all surviving patients comparing preoperative pain scores with scores at 2, 4, and 6 months showed that all patients had an increase in pain at all points irrespective of randomized status (Table 5). The magnitude of this increase was greater, however, in the patients receiving placebo. At no time during follow-up did the mean pain score for patients receiving alcohol without preexisting pain surpass the 3 level set as an arbitrary point of significant pain. The mean number of months without significant pain was 7.2 months in the alcohol group and only 3.0 months in the placebo group ($p < 0.0001$). Only 46% of patients receiving alcohol ever required significant doses of narcotic pain medications (greater than 10 mg IM morphine) compared with 68% of placebo patients ($p < 0.05$). Finally, 56% of patients receiving alcohol splanchnicectomy never reported significant pain until death compared with only 34% of patient in the saline group ($p < 0.05$).

Pain Assessment in Patients with Preexisting Pain

Mean pain scores at the preoperative, 2- and 4-month follow-up and the final assessment for those patients

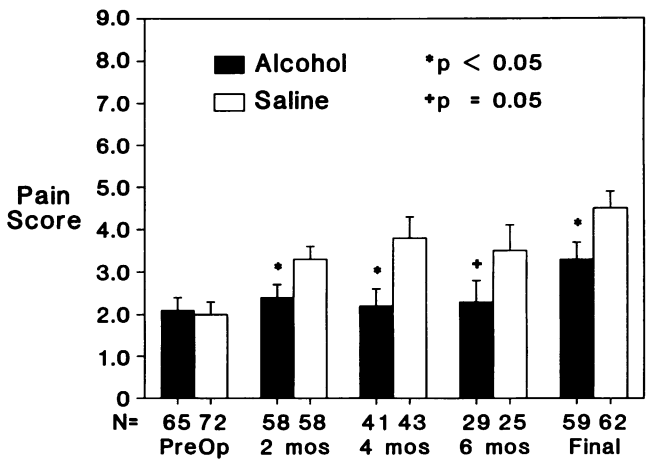

Figure 3. Mean pain scores measured at the preoperative, 2-, 4-, and 6-month, and final assessments for all randomized patients surviving at each point.

Table 4. SERIAL PAIN ASSESSMENT FOR ALL RANDOMIZED PATIENTS (PAIRED ANALYSIS)

Alcohol			Saline		
N = 58	Pre = 2.2 ± .4	2 mos = 2.4 ± .3	N = 57	Pre = 1.9 ± .3	2 mos = 3.4 ± .4*
N = 41	Pre = 1.7 ± .4	4 mos = 2.2 ± .4	N = 43	Pre = 1.2 ± .3	4 mos = 3.8 ± .4*
N = 29	Pre = 1.3 ± .4	6 mos = 2.3 ± .5†	N = 25	Pre = 1.1 ± .3	6 mos = 3.5 ± .6*

* $p < .001$. † $p < .05$ versus Pre.
Pre = Preoperative; range = 0 (no pain) – 10 (severe pain).

with preexisting pain are shown in Figure 5. Alcohol significantly reduced the mean pain score at all points of assessment when compared with control patients. Paired analysis of serial pain assessment for all surviving patients is shown in Table 6. Alcohol injection significantly reduced pain scores at both the 2- and 4-month periods when compared with the preoperative pain score. Patients receiving saline had no change in pain score at 2 months but had significantly increased pain scores at 4 months. Patients receiving alcohol had a mean of 3.3 months pain-free (pain score less than 3) compared with 0.8 months for the saline patients ($p < 0.05$). Seventy percent of patients with preexisting pain receiving alcohol had a decrease in narcotic requirement compared with 0% of the placebo patients ($p < 0.001$). Significant pain did recur before death, however, in 13 of the 20 patients (65%) who received alcohol. All patients in the saline group had significant pain at the time of death. This difference was statistically significant ($p < 0.05$).

Analysis of Mood and Disability Due To Pain

Analysis of scores for patient mood showed a trend to improved mood in patients receiving alcohol; however, this difference did not approach statistical significance for any of the groups. In general, a worsening of mood, or depression, was observed in most patients with progression of disease.

Paired assessment of disability due to pain did increase significantly at 4 and 6 months after placebo splanchnicectomy for all randomized patients. Furthermore, the subgroup of patients without preoperative pain receiving saline also reported increased disability at 2, 4, and 6 months. A similar increase in disability was not observed in patients receiving alcohol injection. In patients with significant preoperative pain, disability was high (range 5.6–7.4). A trend to lower disability scores was observed by paired serial assessment in those patients receiving alcohol but did not reach statistical significance ($p < .15$).

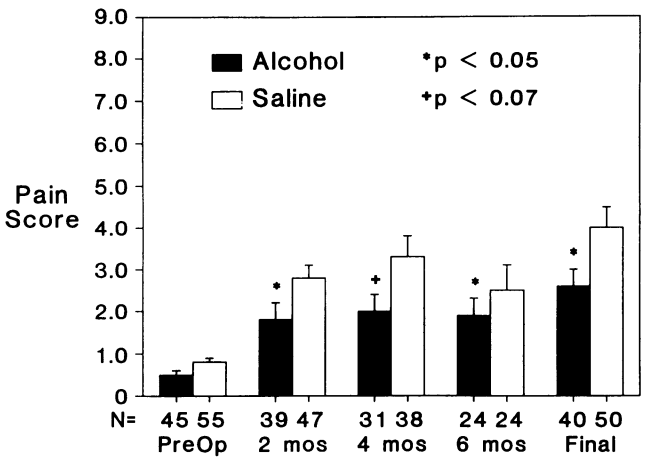

Figure 4. Mean pain scores measured at the preoperative, 2-, 4-, and 6-month, and final assessments for all patients without significant preoperative pain surviving at each point.

Survival

Actuarial survival curves from the time of hospital discharge are shown for all randomized patients (Fig. 6) and for those patients without significant preoperative pain (Fig. 7). No significant difference between the two study groups was observed in either of these survival curves.

The survival curves for those patients with significant pain are shown in Figure 8. Alcohol splanchnicectomy was associated with a marked improvement in survival when compared with saline placebo ($p < 0.0001$). These two subgroups were analyzed with respect to age, tumor location, tumor stage, operation performed, the use of chemo- and radiation therapy, baseline mood, and disability. No significant difference was apparent in any of these comparisons.

DISCUSSION

Pancreatic cancer is currently the fifth leading cause of cancer-related death in this country. Despite improvements in the results of resectional therapy and promising data concerning adjuvant treatment, most series report that the majority of patients are unresectable for cure at the time of diagnosis. Therefore, palliation of symptoms is of primary importance in the majority of patients. As

Table 5. SERIAL PAIN ASSESSMENT FOR PATIENTS WITH NO PRE-EXISTING PAIN (PAIRED ANALYSIS)

Alcohol			Saline		
N = 38	Pre = .4 ± .1	2 mo = 1.7 ± .4*	N = 47	Pre = .9 ± .2	2 mo = 2.8 ± .4†
N = 31	Pre = .4 ± .1	4 mo = 2.0 ± .4*	N = 38	Pre = .8 ± .2	4 mo = 3.3 ± .5†
N = 24	Pre = .4 ± .1	6 mo = 1.9 ± .4*	N = 24	Pre = 1.0 ± .2	6 mo = 3.5 ± .6†

* $p < .01$. † $p < 0.001$ versus Pre.
Pre = Preoperative; range = 0 (no pain) – 10 (severe pain).

with curative therapy, advances in palliative management have also been observed; however, one major symptom complex, pain, has been neglected. Depending on the location of the tumor, pain can be a prominent symptom at presentation. In past series, up to 90% of patients have reported abdominal and/or back pain at the time of presentation.[16] More recently, perhaps with a greater awareness of the diagnosis, the percentage of patients with pancreatic cancer presenting with pain has decreased. Recent studies from the Memorial Sloan Kettering Cancer Center[17] have shown that 40% of patients with pancreatic cancer report no pain at the time of referral, and another 30% have only minimal complaints of pain. Moderate to severe pain was present in 30% of patients with only 10% of patients in the latter category. The results of our initial assessment of pain are similar with only 37 of 137 patients (20%) reporting significant pain, as assessed by a similar technique (visual analogue scales). Yet by the time of death, the vast majority of patients with unresected pancreatic cancer will experience significant pain.

Currently, two primary treatment modalities are used to manage pain due to unresectable pancreatic cancer. A number of series have reported the impact of external beam radiation therapy on pain with symptomatic improvement described in one-third to three-fourths of patients.[18–20] Unfortunately, many of these reports did not use quantitative measures of pain assessment or perform serial assessment of pain relief at regular intervals. In one of the few studies in which the issue of pain management was specifically addressed,[20] only 31% of patients were able to discontinue pain medications for an unspecified amount of time after completion of radiation therapy. Moreover, pain relief with radiation may not occur until several weeks after initiation of therapy, therefore leaving the patient with significant pain through much of their limited life expectancy. Currently, no series has provided a randomized comparison of the use of radiation therapy versus treatment with oral medications for pain control in patients with unresectable pancreatic cancer.

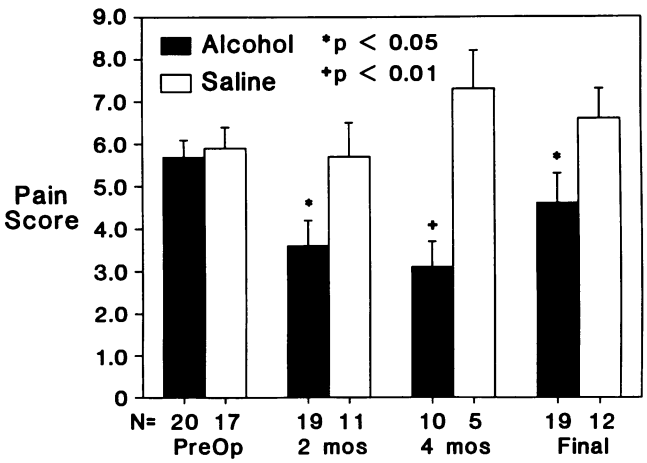

Figure 5. Mean pain scores measured at the preoperative, 2- and 4-month, and final assessments for all patients with significant preoperative pain surviving at each point.

The second major modality for pain control in patients with unresectable pancreatic cancer is percutaneous celiac nerve block performed with either fluoroscopic or CT scan guidance. Pain relief can be achieved in 80–90% of patients,[21–23] but correlations with pain site, extent of disease, and previous therapies have not been made. Similarly, quantitative pain assessment and serial evaluations have not been reported. A review of the English literature over the last 25 years for the use of celiac plexus block for pancreatic cancer found 15 series reporting 480 patients.[24] Although the report appeared to show pain control being achieved in 70–95% of patients, a number of major deficiencies in each study existed, leading for the authors to call for randomized trials for assessment of this technique.

The use of intraoperative chemical splanchnicectomy for unresectable pancreatic cancer was first introduced by Copping and colleagues in 1969.[10] In their 1978 report of 41 patients,[11] 88% of the patients with pain due to pancreatic cancer experienced relief of pain postoperatively. Most of these patients underwent palliative biliary and gastrointestinal bypass at the same operation. These results were compared with a group of historical controls, in which only 21% of patients had pain control

Table 6. SERIAL PAIN ASSESSMENT FOR PATIENTS WITH PRE-EXISTING PAIN (PAIRED ANALYSIS)

Alcohol			Saline		
N = 19	Pre = 5.9 ± .4	2 mos = 3.6 ± .7*	N = 11	Pre = 6.1 ± .7	2 mos = 5.7 ± .8
N = 10	Pre = 6.1 ± .6	4 mos = 3.1 ± .7†	N = 5	Pre = 4.8 ± .9	4 mos = 7.3 ± .9‡

* $p < 0.05$. † $p < 0.02$. ‡ $p < 0.01$ versus Pre.
Pre = Preoperative; range = 0 (no pain) – 10 (severe pain).

after similar palliative procedures. No complications of chemical splanchnicectomy were reported. Since 1978, other authors have advocated chemical splanchnicectomy for the palliation of pain due to unresectable pancreatic carcinoma with anecdotal studies describing successful control of pain in the majority of patients.[12,13] Despite these reports, a prospective, randomized, placebo-controlled study of this treatment has not been performed previously. Such studies remain essential to determine the benefits as well as the complications of this procedure in the overall management of patients undergoing laparotomy for unresectable pancreatic cancer. Finally, the role of chemical splanchnicectomy in patients with unresectable pancreatic cancer without preoperative pain has never been addressed.

The results of this randomized, prospective, placebo-controlled double-blind study performed with standard quantitative measures of pain assessment clearly demonstrate the usefulness of intraoperative chemical splanchnicectomy. In this study the mean pain scores of all randomized patients, as well as the subgroups with and without significant preoperative pain were significantly lower in patients receiving alcohol splanchnicectomy when compared with saline controls. Furthermore, paired analysis has demonstrated that chemical splanchnicectomy with alcohol markedly reduces the extent of pain and postoperative narcotic requirement in patients with significant preoperative pain.

The results of chemical splanchnicectomy in those patients without preexisting pain are less dramatic. Although pain scores were significantly reduced when compared with saline controls, pain did increase over time. However, at no time did mean pain scores in patients receiving alcohol increase to the level of marked to severe pain. Furthermore, the need for narcotic pain medications was avoided in almost half of the patients receiving alcohol, and over half reported no significant pain up to their death.

Unfortunately, the effects of alcohol splanchnicectomy are not permanent. Almost two-thirds of patients with significant preoperative pain, which had been relieved by alcohol block, had moderate to severe pain recur before death with many cases returning to or exceeding the preoperative level. The data suggest that approximately 3 to 4 months of minimal to mild pain might be expected before the return of severe symptoms. Fortunately, our findings would also suggest that percutaneous celiac axis block can relieve pain in most of these patients, therefore, improving the quality of their remaining life.

The results for assessment of mood and disability due to pain were less well defined. Although no differences between groups in raw scores were observed, serial paired analysis suggested that patients receiving the alcohol block continued to function at or near their preopera-

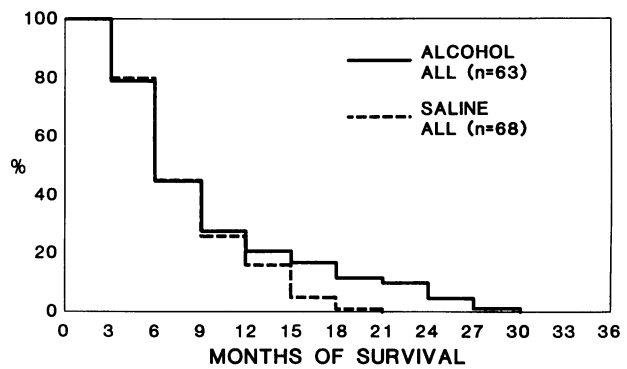

Figure 6. Kaplan-Meier survival curves determined from the time of hospital discharge for all patients.

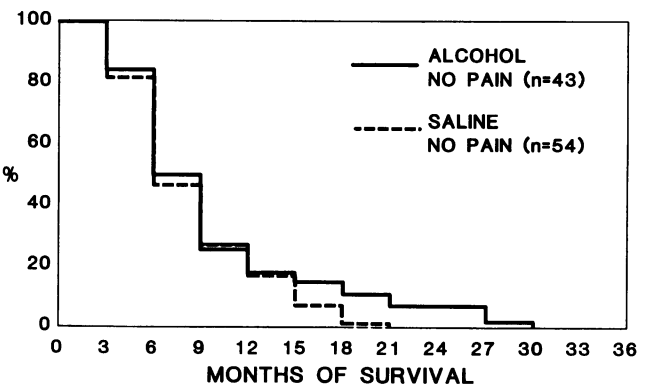

Figure 7. Kaplan-Meier survival curves determined from the time of hospital discharge for patients without preoperative pain.

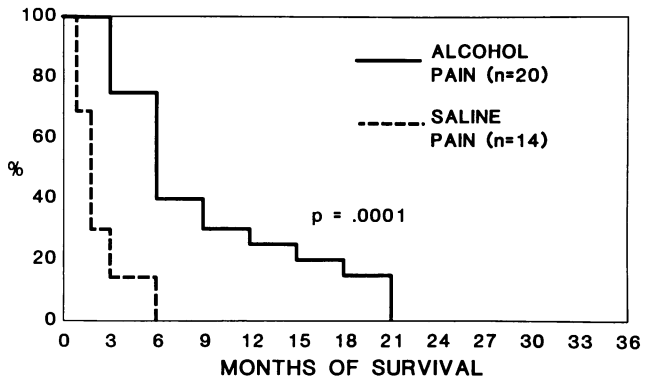

Figure 8. Kaplan-Meier survival curves determined from the time of hospital discharge for patients with significant preoperative pain.

tive level, while progressive deterioration in disability score was reported in the placebo group. Overall scores for mood tended to worsen over time with progression of disease for all patients regardless of randomization status.

An unexpected finding of this study was a highly significant improvement in actuarial survival observed in patients with preoperative pain who received alcohol chemical splanchnicectomy. No other reason for this difference with respect to patient characteristics, operative management or findings, or postoperative treatment was apparent. Disabling constant pain associated with unresectable pancreatic carcinoma is of considerable psychologic and social concern and may be associated with progressive physical deterioration leading to a loss of will to survive. The demoralized, debilitated patient with chronic pain might, therefore, be more likely to experience malnutrition and complications of immobility such as pneumonia and deep venous thrombosis. Achievement of better pain control with chemical splanchnicectomy may prolong life. However, this important observation needs verification by other studies.

In conclusion, the routine use of intraoperative chemical splanchnicectomy with alcohol is suggested for all patients with unresectable pancreatic cancer.

Acknowledgments

The authors thank the members of the surgical staff for participation in the study, the operating room nurses at the Johns Hopkins Hospital for their role in the randomization and careful preparation of the blinded solution, Anne Serna for preparation of the manuscript, and David Goldsborough for assistance in data entry.

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